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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/534,946	03/24/2000	Frank R. Ruderman	MBHB00-203	1964

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EXAMINER	
BLECK, CAROLYN M	

ART UNIT	PAPER NUMBER
3626	

DATE MAILED: 11/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/534,946	RUDERMAN ET AL.	
	Examiner	Art Unit	
	Carolyn M. Bleck	3626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-28 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-28 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Notice to Applicant

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 13 September 2005 has been entered. Claims 22-28 and 38 are pending. Claim 38 has been amended.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 22, 24-28, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levin et al. (5,724,580) in view of Otvos (6,576,471), Krauss et al. (5,925,229), and Applicant's Background of the Art (page 1 of specification).

(A) As per claim 38, Levin discloses a system for managing coronary disease data (reads on "managing cardiovascular healthcare information") (col. 1 lines 9-18, col. 2 lines 39-45 and 50-57, and col. 11 lines 12-15) comprising:

(a) a centralized data management center for maintaining a record of data received by and transmitted from relational databases relating to coronary disease data, wherein the records include patient diagnosis and treatment information collected over time, wherein the processing means at the centralized data management center provide for analyzing patient test results using a coronary wellness master algorithm and artificial intelligence, such as analyzing ECG information, lipid data, including total cholesterol, LDL cholesterol, and HDL cholesterol, and blood pressure of a patient (Fig. 3 and 25A, col. 5 lines 1-36, col. 6 lines 3-28, col. 7 lines 55-63, col. 7 line 64 to col. 8 line 7, col. 8 line 21 to col. 39, col. 10 lines 3-15, col. 10 lines 3-15 and lines 50-55, and col. 12 line 46 to col. 14 line 10), wherein the processing means runs a lipid classification algorithm by inputting patient's LDL and HDL cholesterol values and checking the patient values against the upper limit for normal LDL and HDL cholesterol values, wherein the normal values are stored in the databases at the centralized data management center (Fig. 1-2, 4, and 11-15, Abstract lines 11-14, col. 5 lines 25-37, col. 8 line 21 to col. 9 line 40, col. 10 lines 56-57, and col. 11 lines 5-10);

(b) a monitor displaying a menu (reads on "data entry interface") for entering all known and required information, including patient information such as name, birth date, sex, height, and weight, and test results, such as lipid data, including total cholesterol, LDL cholesterol, and HDL cholesterol, and storing the

information and test results at the centralized data management center databases (Abstract lines 11-14, Fig. 1-2, col. 4 line 53 to col. 5 line 36, col. 10 lines 50-57, and col. 11 lines 5-10); and

(c) processing means at the centralized data management center for analyzing patient test results using a coronary wellness master algorithm and artificial intelligence, such as ECG information, lipid data, including total cholesterol, LDL cholesterol, and HDL cholesterol, and blood pressure of a patient (reads on "diagnostic engine") (col. 7 lines 55-63, col. 8 line 21 to col. 39, col. 10 lines 3-15, col. 10 lines 3-15 and lines 50-55, and col. 12 line 46 to col. 14 line 10), wherein the algorithm correlates test results with risk factors for coronary artery disease and possible treatment recommendations with regard to antischemic therapy, hypolipidemic therapy, antihypertensive therapy, antithrombotic therapy, diabetes, smoking cessation, body weight, and exercise (Fig. 25A-B and col. 10 lines 3-15), wherein an example of the correlation of risk factors includes running a classification of a patient into either an HDL cholesterol acceptable class or a HDL cholesterol low class or HDL elevated class (Fig. 25A-B and col. 8 lines 20-60).

In addition, Levin includes within Figures 11-15 measuring HDL and LDL levels using the units of mg/DL and then classifying the patient into an appropriate class, either an elevated class or optimal class based on the HDL and LDL levels (col. 8 lines 21-47). It is noted that HDL and LDL levels are sub classes of a patient's total cholesterol (Fig. 11-15 and col. 8 lines 21-47).

Levin fails to expressly disclose test results of concentration of subclasses of LDL and subclasses of HDL from cardiovascular patients.

Otvos discloses generating lipoprotein measurement values for a patient's blood sample, the lipoprotein measurement values including a plurality of lipoprotein subclass variable measurements, including LDL size, LDL concentration (reads on "concentration of subclasses of LDL"), large HDL concentration (reads on "concentration of subclasses of HDL"), large VLDL concentration, LDL-C, and HDL-C (see Fig. 2: 71), comparing the plurality of patient lipoprotein subclass variable values with respective predetermined test criteria for determining whether the subclass variable values are associated with a higher or lower risk of developing coronary heart disease, evaluating the lipoprotein measurement values and generating a reduced target value or values for what represents an optimal or low risk value for selected lipoprotein constituents to provide a patient-specific treatment guideline based on the presence of predetermined risk criteria, and automatically generating personalized lipoprotein-based reports for patients (Fig. 1: 32, 32a, 33, 33a, 33b, 43, 43a, 43b, Fig. 2, 2A, 3, 4, 5, 7, 8, 9, 11, 14, col. 3 line 32 to col. 4 line 5, col. 5 lines 22-45, col. 11 lines 12-46, col: 16 lines 48-62, col. 19 line 55 to col. 20 line 40).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to include the aforementioned lipoprotein subclass variable measurements of Otvos within the system taught by Levin with the motivation of accurately diagnosing a patient with coronary artery disease by

using a comprehensive set of data thus allowing a physician to effectively manage coronary artery disease (Levin; col. 2 lines 15-60) and utilizing subclass information for lipoproteins because subclass information provides a more reliable indicator of a patient's risk to develop coronary heart disease (Otvos; col. 1 lines 55-65).

As per the recitation of "identifying patients who do not have hyperlipidemia but are in need of treatment", Otvos teaches using NMR spectroscopy to obtain subclass information, wherein the subclass information is a more reliable indicator of a patient's risk to develop coronary heart disease, wherein various subclasses of lipoproteins may provide more reliable markers of the metabolic conditions that predispose individuals to a greater or lesser risk of heart disease (col. 1 line 42 to col. 2 line 11). Further, Otvos teaches that without an NMR subclass profile, a patient with a specific type of lipid profile may have been overlooked as a candidate for further review or potential behavior altering counseling (or even drug therapy) because of the number of borderline lipid measurement results (col. 16 lines 48-62). It is respectfully submitted that using an NMR subclass profile, such as that disclosed by Otvos, is a means for identifying patients who do not have hyperlipidemia but are in need of treatment (i.e., patients who would ordinarily be overlooked). The motivation being to improve the health care of patients by using the subclass information as a more reliable indicator of a patient's risk to develop coronary heart disease (col. 1 line 42 to col. 2 line 11).

Levin and Otvos fail to expressly disclose the subclasses of LDL particles and subclasses of HDL particles being levels determined by segmented gradient gel electrophoresis.

Krauss discloses using segmented gradient gel electrophoresis to determine the subclasses of LDL particles and HDL particles (col. 1 line 15 to col. 2 line 47, col. 14 line 61 to col. 16 line 22)

At the time the invention was made, it would have been have been obvious to one of ordinary skill in the art to combine the features of Krauss within the system of Levin and Otvos with the motivation of providing a rapid and inexpensive assay for quantifying LDL and HDL subclasses (Krauss; col. 2 lines 49-67).

As per the recitation of "the particle subclasses including HDL2b," it is respectfully submitted that the Applicant's Background of the Invention discloses that "the art describes cardiovascular risk factors such as... lipid profiles including LDL and HDL and subclasses (fractions) of LDL and HDL. Methods for measuring these factors and relating them to patient treatment are also known." The Examiner respectfully submits that it is well known in the art that HDL2b is a major subclass of high-density lipoproteins. It would appear from Applicant's Background of the Invention that this would be a "cardiovascular risk factor" that is well known in the art. The motivation for measuring this factor using segmented gradient gel electrophoresis being to provide an ever more nuanced picture of the cardiovascular disease process that will enable doctors to better

assess which patients are at risk for heart disease, stop heart attacks before they happen and develop more effective, customized treatment plans.

(B) As per claim 22, Levin discloses a monitor displaying a menu (reads on "physician data access interface") for providing a physician, such as a cardiologist, with the ability to access, display, review, and transfer information stored at the centralized data management center (col. 2 lines 1-15, col. 5 lines 49-67, and col. 11 lines 1-10).

(C) As per claim 24, Levin discloses a storage means that stores information related to coronary illness risk factors which have been established based on empirical data, wherein the information allows physicians to determine the effectiveness of diagnoses and treatments as the information is gathered over time and as the pool of treated patients increases (Abstract lines 11-14, col. 6 line 3-15, and col. 10 lines 3-15). It is respectfully submitted that the storage means disclosed by Levin is a form of a knowledge base as the data collected in the database is a collection of knowledge of specialists such as cardiologists, and the data collected will be used to effectively identify patients at significant risk of sudden death and to quantify the success of various treatments both for the patient pool and fro particular patients (col. 6 line 3-15).

(D) As per claims 25-27, Levin discloses processing means at the centralized data management center for analyzing patient test results using a coronary

wellness master algorithm and artificial intelligence, wherein patient test results include ECG information, lipid data, including total cholesterol, LDL cholesterol, and HDL cholesterol, and blood pressure of a patient, and wherein the test results determine base numbers for a patient (reads on "diagnostic engine" and "baseline determination for ongoing therapy monitoring") (Fig. 3, col. 5 lines 25-36, col. 6 lines 16-28, col. 7 lines 55-63, col. 7 line 64 to col. 8 line 7, col. 8 line 21 to col. 39, col. 9 lines 18-39, col. 10 lines 3-15, col. 10 lines 3-15 and lines 50-55, and col. 12 line 46 to col. 14 line 10) wherein:

(a) the algorithms correlate test results with possible treatment recommendations with regard to antischemic therapy, hypolipidemic therapy, antihypertensive therapy, antithrombotic therapy, diabetes, smoking cessation, body weight, and exercise (Fig. 25A-B and col. 10 lines 3-15);

(b) the algorithms correlate test results with possible or recommended diagnoses, such as such as whether the levels of total cholesterol, LDL cholesterol, and HDL cholesterol are acceptable or not, and the diagnosis classification for blood pressure of a patient, wherein the classification includes normal, high-normal, mild hypertension, moderate hypertension, severe hypertension, and very severe hypertension (col. 8 line 21 to col. 9 line 39, col. 10 lines 3-15, and col. 11 line 10-15); and

(c) the algorithms correlate diagnosis information with possible or recommended treatments (Fig. 25A-B, col. 5 lines 16-37, col. 6 line 16 to col. 7 line 47, col. 8 line 21 to col. 9 line 39, and col. 10 lines 3-15).

3. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Levin et al. (5,724,580), Otvos (6,576,471), Krauss et al. (5,925,229), and Applicant's Background of the Art (page 1 of specification) as applied to claim 37, and further in view of Surwit et al. (6,024,699).

(A) As per claim 23, the relevant teachings of Levin and Otvos, and the motivation for their combination is as discussed in the rejections above, and incorporated herein.

Levin, Otvos, and Krauss fail to expressly disclose a communication system allowing the physician to communicate cardiovascular healthcare management information to a patient. However, Levin includes communicating coronary illness information to and from a physician, such as a cardiologist, via communication network (Fig. 1-3 and 25A-25B, col. 2 line 62 to col. 3 line 10, col. 4 lines 31-55, col. 7 lines 33-47, and col. 7 line 64 to col. 8 line 7).

Surwit discloses a system for monitoring, diagnosing, prioritizing, and treating chronic medical conditions of a plurality of remotely located patients, wherein treatment information is provided to a patient via a computer network (Fig. 1 and 3, col. 2 lines 38-55, col. 3 lines 24-38, col. 6 line 27 to col. 7 line 13, col. 9 lines 24-58, col. 18 line 45 to col. 19 line 40).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to combine the aforementioned component of Surwit within the system taught collectively by Levin, Otvos, and Krauss with the motivation of quickly and easily monitoring patients and automatically identifying

a patient with a medical condition, quickly preparing and revising medicine dosages for a patient and then efficiently communicating revised dosage information to a patient (Surwit; col. 2 lines 25-35), and reducing the costs of medical treatment by providing a fast, effective technique for providing comprehensive management of coronary patients based on risk factors including up to date diagnoses and treatment information (Levin; col. 2 lines 16-49).

Response to Arguments

4. Applicant's arguments with respect to claims 22-28 and 38 have been considered but are moot in view of the new ground(s) of rejection.

(A) All of the limitations which Applicant disputes as missing in the applied references, including the features newly added in the 13 September 2005 amendment, have been fully addressed by the Examiner as either being fully disclosed or obvious in view of the collective teachings of Levin, Otvos, and Krauss, based on the logic and sound scientific reasoning of one ordinarily skilled in the art at the time of the invention, as detailed in the remarks and explanations given in the preceding sections of the present Office Action, and incorporated herein. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Bleck whose telephone number is (571) 272-6767. The Examiner can normally be reached on Monday-Thursday, 8:00am – 5:30pm, and from 8:30am – 5:00pm on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Thomas can be reached at (571) 272-6776.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

6. **Any response to this action should be mailed to:**

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Or faxed to:

(571) 273-8300 [Official communications]

(571) 273-8300 [After Final communications labeled "Box AF"]

(571) 273-6767 [Informal/ Draft communications, labeled "PROPOSED" or "DRAFT"]

Hand-delivered responses should be brought to the Knox Building, Alexandria, VA.

CB
October 20, 2005

JOSEPH THOMAS
SUPERVISORY PATENT EXAMINER
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